



Description of BE891141

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#### PREPARATION Of a GEL ABLE TO CONVEY GASES

The present invention relates to a method of preparation of a composition gelled containing organic liquid inert, able to convey a gas. It also refers to the composition thus obtained, which can be used in particular in medicine and in a certain number of industries of which that of the cosmetic products. One knows many organic liquids iner-

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a capacity solvent raised with respect to/gases like oxygen feels, nitrogenizes, carbon dioxide, gases inert, and their mixtures, including the air. Among the many groups of inert organic liquids, presenting these properties, are oils of silicone with low viscosity and fluorocarburés liquid, nonmiscible with water. These groups of liquid are described in patent U.S.

N [deg.] 3.850.753 of Chibata and coll, concerning the culture of micro-organisms aerobic. However, it is not made mention in this patent of emulsions or gelled compositions.

Other fluorocarburés, their emulsions and their properties are described in patents U.S. following:

N [deg.] 4.220.606 and N [deg.] 4.143.079 of R.E. Moore; N [deg.] 4.105.798 and N [deg.] 4.041.086 of Moore and coll; N [deg.] 3.911.138 of L.C.

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coll.; and N [deg.] 3.641.167 of Moore and coll. There is also a process of David C. White for the treatment of wounds, such as burns, by the establishment of contact between those with a liquid fluorocarburé, either directly, or via a sponge, or in the form of foam, of vaporization or freezing. But it is not there question of a specific composition of freezing, or of very proceeded to prepare it.

One knows techniques of separation of various substances in the form of particles, starting from the aqueous medium in which they were formed or have

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described the insulation in the form of dry powder, of the therapeutic agent derived from latex natural of *Lactuca*, which consists in letting break the emulsion at rest, then to filter or centrifuge, to separate the aqueous solution, containing the active component.

Moreover, it is known that various gel is produced starting from aqueous suspensions, by precipitation, decantation, filtration (including filtration by membrane) and centrifugation. These products are commonly insulated in the form of dry substances, and are called "gel" apparently because in contact with water they pass by again in a semi-solid state, somewhat plastic or inflated. They have a high porosity and are used for various uses, according to their origin, their porosity and their aptitude for swelling. Among these substances the gelatine-carboxyméthyl cellulose complexes of patent U.S. appear. N [deg.] 2.824.092; proteinate hydrogels of soya of patent U.S. N [deg.] 3.218.307; the gelatinous, flocculent product obtained by fermentation of a natural polysaccharide, followed centrifugation, as in patent U.S. N [deg.] 3.096.293; ethers of hydroxy lower alkyl of galactomannanes, produced in the form of hydrocolloides stable, dry, by filtration and centrifugation, as in patent U.S. N [deg.] 3.326.890; dry gel of agarose of patent U.S. N [deg.] 3.527.712; and produced silica gels

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But, in any de' these patents is not described or is suggested the concentration of an emulsion, accompanied by the formation by a gelatinous substance, nor the preparation of a gelatinous substance containing an inert organic liquid, nonmiscible with water, vehiculor of gas.

The present invention makes it possible to obtain agents véhiculors of gas, in the form of gel, having the advantage on the emulsions of a transport capacity of gas per unit of volume, quite higher, since a strong proportion of the conveying substance not-gas, namely water, is eliminated from it. The method of preparation of the new freezing according to the invention consists in mixing a liquid organic, inert, nonmiscible with water, able to convey a gas, with water and an adapted emulsifying agent, in

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ser formation of the emulsion, to concentrate the emulsion carried out, to involve the formation of a phase freezing and a liquid phase, and to separate partly or entirely the liquid phase from the phase freezing.

Resulting freezing is a stable composition, which can be used for example like pomade, balsam or ointment, for the treatment of wounds or irritations of the skin, or under any condition requiring the presence of a gas such as oxygen.

The term "freezing", used here, indicates a semi-solid substance, of homogeneous appearance, which can be elastic and to have the aspect of a frost (like gelatine), or to be more or less rigid. Contrairement T to what is indicated in the patents referred to above, the "gel" according to the invention cannot be brought to the state of particles dry, porous, nor cannot present, in contact with water, an appreciable degree of swelling. This is why here "freezing" is used in the direction more general of a gelatinous nature or aspect of frost.

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strongly or completely fluorinated stearic acid, which generally arises, but not necessarily, at temperature and environmental pressure, in the liquid state, and which has the capacity to convey gases such as oxygenates/carbon dioxide. "Strongly fluorinated" means that the majority of the hydrogen atoms of compound were replaced by atoms

of fluorine, so that an additional replacement strongly does not increase gas the conveying capacity of the substance. It is thought that this level is reached when it

<EMI ID=7.1>

by fluorine atoms. In patents U.S. N [deg.]

3.911.138 and N [deg.] 4.105.798, mentioned above, the aptitude to convey oxygen depends on the solubility of a gas as oxygen in the substances. One suggests in these patents that the perfluorées substances absorb 10 to 100 ml of oxygen/100 ml of substance, with 25 [deg.]C, under 760 mm of mercury. However, it is preferable to have a rate of replacement of the hydrogen atoms of at least

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Are appropriate like fluorinated substances, in accordance with the invention, in particular of the substances indicated approximately under the name of cyclic perfluorohydrocarburés, like their derivatives. One can quote as examples of the polycyclic of fluorine, chemically inert compounds,

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derived like methyl, dimethyl, éthyl-, diéthyl-, éthyldiméthyl-, triéthyl- or méthyléthyl-adamantane; of tetrahydrodicyclopentadiene; methyl or dimethyl-bicyclooctane of tétrahydrobinor-S; methyl or triméthyl-dia-

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and similar like their mixtures. Are also appropriate perfluorotributylamine, perfluoro butyl-2 tétrahydrofuranne, perfluoro butyl-2 furan, perfluoro N-heptane, perfluoronaphthalene, perfluoro methyl-1 naphthalene, perfluoro N-methyl morpholine, and perfluoro methyl-1 décaline, as well as perfluoroéthers like ether tétrafluoro-1,2,2,

<EMI ID=11.1> décanol).

Some of the fluorine atoms of the substances ci dessus can be replaced by atoms of other halogens as bromine. Appear, for example, among these compounds of the derivatives monobromés like bromo-1 pentadéca-

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hexane, bromo-1 pentadécafluoro octane, and bromo-1 pentadécafluoro isopropyl-3 cyclopentane, like their dibromés analogues.

One can use, in accordance with the invention,

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lement brominated, as well as mixtures of these various perfluorés compounds.

Those of the preceding fluorinated compounds, which are solid at ambient temperature, can be dissolved in an adapted solvent, or other liquid perfluorocarbures at ambient temperature, and the resulting mixture can be used to form the émulsionné freezing according to the invention. By "liquid" one hears in this description, when they are fluorocarbures, as well a liquid fluorocarbure in oneself at the ambient temperature, that a solution of a solid fluorocarbure in a fluorocarbonaceous solvent.

Silicone oils usable conformément

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the order from 0,65 to 15 centipoises, as it is the case for the silicone oil "DC-200-1CD" manufactured by Dow Corning Corporation, which has a molecular weight of 316, a density of 0,85, and a capacity solvent with respect to the oxygen of 100 ml/100 ml of liquid with 25 [deg.]C. Other silicone fluids, of Dow Corning Corporation usable in accordance with the invention, are generally indicated by the denomination of fluids "cd. - 200". Chemically, silicone oils are polydiméthyl siloxanes, and are also known as being liquid methyl silicones. Similar silicone fluids/are also manufactured by General Electric Company.

During the first stage of preparation of the gel, the inert organic liquid, gas vehicular are emulsified in water in the presence of an agent emulsion

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its mixture with water and the body fluid, it occurs an effective émulsionnage with stability of freezing; it must be compatible with the body fluid, and does not have to produce harmful effect, when freezing obtained is applied for example to the human skin.

Although one prefers the émulsionneurs nonionic, because they are active out of fresh water and water

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lement to use anion, cation or amphoteric emulsifiers.

Are appropriate in particular like non-ionic emulsifiers, of the alkylphénoxypolyéthoxyéthanols comprising groupings alkyl from 7 to 18 carbon atoms approximately, and of

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and similar; derivatives polyéthoxyethanolic of alkylphénols bound by methylene; agents containing of sulphur as those which one prepares by condensation of 1

with 60, or even more, moles of ethylene oxide with nonyl-, dodécy-, tétradécy-, and T-dodécy-thiol, and mercaptans

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ments nikyle comprises from 6 to 15 carbon atoms; ethylene oxide derivatives of acids carboxylic with long chain like the acids lauric, myristic, palmitic, oleic and similar, or of mixtures of acids as those which one finds in the oil of tall, container of 1 - 60

<EMI ID=19.1> oxide tion similar of ethylene and alcohols to long chain like alcohols octyl-, decyl-, dodecyl- or cetyl; derivatives of oxide of ethylene of made up polyhydroxy etherified or esterified, comprising a hydrophobic hydrocarbon chain, like the monostéarate of sorbitane container from 1 to 60 units of oxyethylene; products of ethylene oxide condensation and amines with long chain or chain ramified like dodécyamine, hexadécyamine and octadécyamine, containing 1

with 60 groupings oxyéthénique; and of the copolymers sequences of oxide of propylene ethylene and oxide, including/understanding a part oxidizes hydrophobic propylene combined with one or more parts oxidizes absorbent ethylene.

Among interesting anion emulsifiers one can quote the ordinary soaps like salts of alkaline metals, ammonium and alkanolamines of acids fatty, including oleate of sodium, potassium palmitate, ammonium stearate, laurate of éthanolamine and similar, as well as acid dehydrated rosin and rosin soaps; synthetic saponaceous substances including/understanding higher sulphonates and aliphatic sulphates like sulphates sodic lauryl, sulphates sodic cetyl, sodic sulfonic paraffin oil salts, salts so-, dic of the acids dodecane-1 and octadécan-1- sulphonate and similar; alkarylsulfonates like isopropylben-

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of sodium; alkaline amide metal salts and esters of sulfonic acids dicarboxylic like sulfosuccinate of sodic dioctyle, sodic N-octadécyld sulfosuccinamide; sulfonic or sulphated alkyl phénoxypolyéthoxyéthanols,

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which the grouping alkyl presents from 4 to 18 carbon atoms, like hexyl, similar N-octyl, tert-octyl, lauryl, hexadécylique and octadécylique and.

Are appropriate like cation emulsifiers, Mo< EMI ID=22.1>

hydroxyéthyl ammonium, stéaroguanamine, produced reaction of ethylene oxide and stéaroguanamine, salts of octadécyamine of the acid octadécylic carbamic and salts of octadécylique guanamine of the carbamic acid octadécylique having reacted with oxide of ethylene, octadécylique rosin amine tétraéthyl glycol, produced reaction of amine with ethylene oxide, and similar. Are also appropriate the undécylimidazoline and its products of reaction with ethylene oxide and propylene oxide; the chlo-

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densation of fatty acids and degraded proteins; sulphate of monostéaryléthylénediamine triméthylammonium; the alkyl benzene imidazolines; the bromide of cetyl py-

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nium; the acetate of octadecylmethylene pyridinium; oxide of laurylureeethylene; sulphate of methyl and dimethyl octadécylique sulfonium; products of condensation of halogénohydrines and amino, polyamines and ammonia;

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oxide sation of ethylene and alkyl phosphonium, the rosin amines condensed with oxide of ethylene and propylene oxide; cetyl.diméthyl chloride benzyl ammonium, chloride dimethyl distéaryl ammon-

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methyl dichloride, méthylodécylique benzyl chloride, dimethyl n-alkyl chloride benzyl ammonium triméthyl ammonium dodécylique xylene (a) (triméthylammonium), bromide of cetyl triméthyl ammonium, and similar.

The amphoteric emulsifiers adapted, according to the invention, include/understand the N-coconut beta-aminopropionate of sodium, the acid N-coconut beta-aminopropionate, disodic N-lauryl beta-iminodipropionate, the salt of dicarboxylic diethanolamine of coconut derivative, the sodic salt of palmitic derivative dicarboxylic, C-cétyle bétatne, and N-lauryl Be-tatne.

The surface-active products of any type containing of fluorine are interesting, that they are ionic

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that, potassium and ammonium perfluoroalkylsulfonates, fluorinated potassium alkylcarboxylates, and the carboxylate perfluoro alkyl of ammonium. With regard to the non-ionic type, one can mention for example

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above, and other surface-active products containing of fluorine, are available in the trade under designations of surface-active FC-93, FC-95, FC-128, FC-143, FC-430 and FC-431, sold by 3M Company.

Certain emulsifiers existing in a natural state, or their derivatives, prove also interesting: they include/understand in particular alginates, of derived from cellulose like the methyl cellulose and carboxymethyl cellulose, of water soluble gums as the gum arabic and the gum adragante, of phospholipides like lecithins, and sterols.

The preferred emulsifiers are non-ionic Pluronic F-68 and Pluronic F-108, as well as phospholipides of the egg yolk. Pluronic are polyoxyethylenes and polyoxypropylenes manufactured by Wyandotte-BASF. Generally, the emulsifier, ionic or non-ionic, is util-

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the composition of total emulsion, or until approximately 5% in weight of water used to form the emulsion. E can

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sionnante can be used each one taken separately, or in combination with several provided that they are compatible from the ionic point of view.

Quantities and proportions of body fluid,

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used to form the emulsion and freezing, can vary largely. In general, the quantities of each component are such as they allow the formation of an emulsion, and they can be easily determined by the expert without excessive experimentation. However, concentration preferred in body fluid

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better from 10 to 50%, the total composition.

In another embodiment of this invention, freezing can be treated in order to contain more oxygen than it would not be differently. Such a technique consists in putting in contact the body fluid with an oxygen supplement, before combining it with the other substances. For example, the body fluid can be subjected, before the émulsionnage, with an environment 11 100% of oxygen, under a pressure equal or higher than 760 mm of mercury. Or, resulting freezing is subjected to an environment of oxygen 100%, which can be with a pressure equal or higher than mercury 760mm.

& top The mixture of body fluid, water and agent emulsifying, is emulsified by any traditional means of mixing, for example manual agitation, ventilation, by

propeller or turbine, colloidal crushing, homogenisation, application of high frequencies, vibration ultrasonic and similar. In the majority of the cases, one operates with temple

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agitation precedents, it can, during the formation

emulsion and/or gel, y to have production of an excess of heat, which must be eliminated by known means, for example cooling envelope. The quantity of mechanical contribution of energy, coming from the various means of agitation, can strongly vary according to, for example, the quantity of substance to be treated, and equipment used.

During the second stage of preparation of the gel, according to the invention, the emulsion is concentrated to give rise to a phase freezing and to a liquid phase. One uses a centrifugation at high speed to this end (ultracentrifugation), for example at the speed of 10.000 with 20.000 turns/minute, the choice speed depending on

the proportion of body fluid in the emulsion (less there is of body fluid plus speed is large).

One obtains a liquid surviving, limpid, and a solid

with consistency of paste, i.e. the phase freezing, which falls at the bottom from the container.

During the third stage, the phase freezing and the liquid phase are separated by deposit, evaporation, dedantation, or filtration, in particular under pressure or vacuum.

Separation can be partial or complete, according to what is necessary for the secondary treatment. Thus for examples, so at this time one wishes to add to the freezing of with

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pharmaceutical, moistening, perfumes, dyes or other known additives of the expert, it can be preferable to leave a little liquid in contact with freezing.

In addition, if a use or an immediate packing is considered, it can be desirable to have a complete separation of the liquid.

The preceding description of the second and third stages constitutes a process of concentration and from separated

<EMI ID=35.1>

tre realized simultaneously by microfiltration (or ultrafiltration). However, microfiltration is effective only for emulsions whose dimension of the particles is relatively large, about more than one micron, because the majority of the membranes of microfiltration of the trade have

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Thus, when the particles of the emulsion are very fine, they can pass through the membrane of microfiltration, and there is no separation. As several of the emulsions according to the invention have particles whose dimension lies between 0,1 and approximately 10 microns, microfiltration constitutes a practical process for simultaneously concentrating the emulsion, in order to form a gel, and to separate this freezing from the surviving liquid phase, resulting. Are appropriate, like membranes of microfiltration, of the products available at Millipore Company and Amicon Corporation, and described for example in patents U.S. N [deg.] 3.615.024 and N [deg.] 3.856.569.

In general, when it is wished, simultaneously, to form freezing, and to separate it from the aqueous phase, it is desirable that the dimension of particle of the emulsion be large. These kinds of emulsions are formed when the components are used in the following proportions:

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These proportions can vary apart from these intervals, according to characteristics' of the body inert fluid and the surface-active product.

One can possibly use jointly with the micro filtration, decantation or vacuum filtration or sou lession. Pressure filtration is preferred with vacuum filtration, because one observes with the course of the latter a tendency to the foam formation.

One can possibly incorporate in the gel according to the invention, an agent antibactérien and/or an antibiotic agent. The agent antibactérien thwarts the development of the aerobic bacteria which can multiply in the presence of freezing, since this one contains great quantities of oxygen. Like agents antibactériens the carboxylic acids quinoline, the nitrofurannes and sulphonamides are appropriate. The suitable agents are those which do not deteriorate freezing, or which are not faded

<EMI ID=38.1> nglucosides, ansacrolides, chloramphenicol and its analogues, lincosaminides, macrolides, nurléosides, oligosaccharides, peptides, phenazines, polyenes, polyethers, tetracyclines and similar. The preceding agents are described with more detail in Encyclopedia off Chemical Technology, Vol. 2, pages 752-1036 and Vol. 3, pages 7-78, 3rd Edition. The agents referred to above, can be built-in in freezing at any stage of its preparation, for example by addition with the liquid component before emulsification (for example by dissolution in water), by dispersion in the emulsion during or afterwards

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tion.

Resulting freezing can be used as ointment, applied to the skin of the higher mammals, including the man, for the treatment of the wounds, contusions or irritations. This freezing can also be formed or incorporated

in a bandage, which is then applied to the skin.

The word "bandage", used here, includes/understands any suitable substance for the setting in contact (including a wound) with freezing, and the maintenance of this contact, for example gauze, bindings, envelopments surgical, and similar.

The examples nonrestrictive following illustrate several embodiments of this intention. EXAMPLE 1

4 G (2 ml) of F-tributylamine (perfluorotributylamine) and

18 ml of water containing 5% in weight of Pluronic F-68 (surface-active agent), are placed in a test tube. The perfluorocarbure is dispersed uniformly in water by vibration with ultrasounds. The test tube, containing this moved Sion similar to milk, is then subjected to a centrifugation with 10.000 turns/minutes during 10 minutes. It results a limpid liquid from it surviving, and at the bottom a solid of the pasty type (freezing). The limpid liquid is elutriated, leaving behind him in the tube freezing. This freezing is removed tube using a spatula and put in another container; it has the aspect of petroleum jelly and weighs 5 G.

This freezing, one adds 5 ml of ethanol: 4 G of F-tributyl-

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milkling, separate from the water-ethanol layer, in the form of a limpid layer liquid, which shows that freezing

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One repeats the preceding procedure, except with regard to the addition of ethanol, and one obtains a gel which one keeps in a mouth flask broad. At the end of

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physical aspect of freezing, such as separation of perfluorocarbure of water, which indicates that freezing is stable.

EXAMPLE 2

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25,65 G of water. This aqueous mixture is added with 3 ml

(6 G) of F-tributylamine. Composition resulting is subjected to vibrations by ultrasounds, which on average gives an opalescent emulsion, whose dimension of the particles is relatively large, approximately 1 to 10 microns. One filters this emulsion under nitrogen pressure close to 1,75 bar, through a microporous membrane of Millipore of apparent size of pore of 0,45 microns. It is formed a gel which remains on the filter, and which one easily transvases in a container of storage.

EXAMPLE 3

One takes again the preparatory technique of example 2 in his principal lines, with this close which one replaces F-tributylamine by of F-triméthylbicyclonane. One obtains a gel of practically equivalent aspect.

EXAMPLE 4

An emulsion is prepared, practically as described in

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ml of water and 5% in weight of Plufonic F-68, addition of 2,5 ml of silicone oil SF 96-50 of General Electric, and vibration by ultrasounds, which gives an emulsion of a milky white. The silicone oil used has a viscosity of 50 centistoke, a density of 0,963, a point flash of 238 [deg.]C, and a point of flow of -55 [deg.]C. This emulsion is then centrifuged at 14.000 turns/minute during 20 minutes, following what a white, pasty gel separates; the fluid is then separated from ce/gel by decantation.

Claims

1. Proceeded of preparation of a gel gas, characterized in that conveys one mixes a liquid organic, inert, nonmiscible with water and able to convey a gas, with water and a suitable emulsifying agent, under conditions of agitation and proportions suitable to support the formation of the emulsion, and one concentrates the emulsion carried out to involve the formation of a phase freezing and a liquid phase, that one separates partially or entirely.